TABLE 5-8

Hemoglobin Variants Found During the Los Angeles Survey

Origin	Number	AS	SS	AC	CC	SC	Others
Black	1205	143	3	23	0	1	2[a]
Spanish surname	8048	30	0	7	0	0	0
Others	1148	15	0	7	0	0	1[b]
TOTAL	10401	188	3	37	0	1	3

[a]Two unidentified β chain variants.
[b]An unidentified γ chain variant.

advantage of readily differentiating conditions such as AA, AS, SS, AC, CC, and SC and, moreover, has the desired advantage of simplicity. Identification of Hb-E, α chain variants such as Hb-G-Philadelphia, and γ chain variants is difficult with this procedure. Differentiation at birth between SS, Hb-S-β-thalassemia, and the Hb-S-HPFH condition is not possible (such a differentiation can also not be made with electrophoretic methods).

Table 5-8 lists the data. Hb-S was found in 8% of the 1205 black infants examined and Hb-C was present in 2%. About 0.5% of the over 8000 "Spanish surname" newborns had an abnormal hemoglobin and the incidence in the remaining category was even higher (2%). The diagnosis of SS and SC in the four newborns was confirmed by macrocolumn chromatography and by analyses of samples obtained at subsequent examinations of these infants.

The Survey on the Islands Malta and Gozo, Malta*

This study concerned cord blood samples of 9541 neonates from both islands of Malta; the samples were collected in collaboration with the obstetric services of several hospitals.

Identification procedures included cellulose acetate electrophoresis (6941 samples) and starch gel electrophoresis (2600) samples. Most samples containing an abnormal variant were also studied in a second laboratory (Augusta, Ga.) using the same and more extensive procedures. Quantitative data were obtained both by macro- and by microchromatography using columns of CM-cellulose (see Chapter 4).

*Data were supplied by Dr. A. Felice, Msida, Malta.

Figure 5-11 illustrates the separation of Hb-F, Hb-A and Hb-F-Malta-I by starch gel electrophoresis. The electrophoresis lasted only a few hours which prevented a clear distinction between the electrophoretic mobilities of this γ chain variant and the Hb-F_X found in some black newborns. Hb-F-Malta-I is the most important abnormality; it was observed in 156 newborns (or in 1.6% of all newborns examined). In addition, one newborn had another γ chain variant (Hb-F-Malta-II which is an $^{A}\gamma$ type) and 5 newborns were heterozygous for the α chain variant Hb-St. Luke's. No β chain variants were observed and Hb-Bart's was absent in all samples. The incidence of Hb-F-Malta-I was the highest on the island of Gozo; the smaller study of 2600 samples which used starch gel electrophoresis showed an incidence of 1.2% in Maltese neonates (28 of 2330 cases examined) and of 4.7% in Gozitans (13 of 270 cases examined).

Quantitative data are presented in Table 5-9. It appears that Hb-F-Malta-I comprises about one-quarter of the total Hb-F in the heterozygote; the data, however, show a wide range which remains unexplained. The quantity of the γ chain variant in the Hb-F-Malta-II heterozygote was a low 5%. Figure 5-12 summarizes quantitative data of five different γ chain variants in the respective heterozygotes. Four distinct groups are recognized, namely a $^{G}\gamma$ type present for 22.5%, a $^{G}\gamma$ type present for 13.5%, $^{A}\gamma$ types present for 12.5%, and an $^{A}\gamma$ type present for 5%. This observation has been the basis for the assumption of the existence of perhaps as many as four γ chain structural loci per chromosome [13].

TABLE 5-9

The Quantities of Hb-F-Malta-I in Cord Blood Samples of Heterozygotes

Method	Number	% F-Malta-I[a] of Total Hb	% F-Malta-I[a] of Total Hb-F
CM-Cellulose (macro procedure)	37	17.9 ± 3.1 (12.1-20.8)	22.4 ± 3.0 (15.8-27.3)
CM-Cellulose (micro procedure)	12	19.9 ± 3.2 (14.3-37.5)	21.5 ± 3.2 (20.8-41.1[b])

[a]Mean value with standard deviation and range.
[b]One sample with 41.1% Hb-F-Malta-I was studied by both methods; the 41.1% is probably in error.

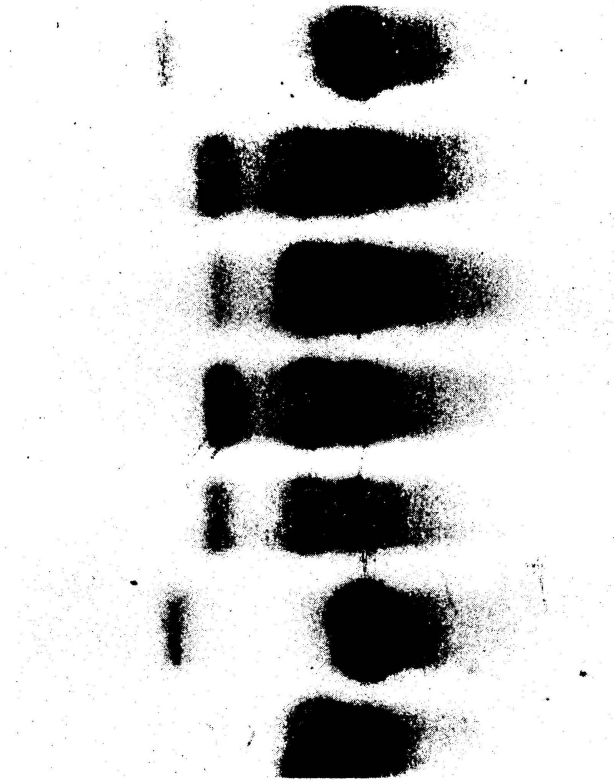

FIG. 5-11. Starch gel electrophoretic examination of cord blood hemoglobins. The two samples with Hb-F_x are from black newborns and the two with Hb-F-Malta-I from Gozitan infants. Both variants are of the $G\gamma$ type.

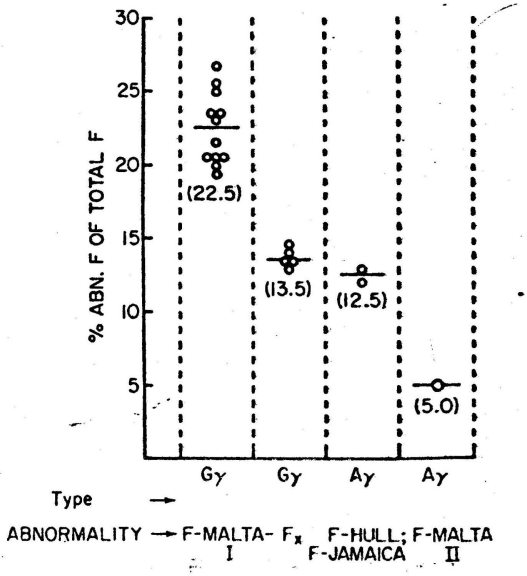

FIG. 5-12. The relative amounts of fetal hemoglobin variants which are abnormal in γ chains. Values are from individual heterozygotes aged 1 to 120 days. Numbers in parentheses are the mean values.

The Survey in Bangkok, Thailand*

This survey is continuously conducted and concerns several thousand neonates. The method used is starch gel electrophoresis in Tris-EDTA-boric acid buffer, pH 8.6, the gels being stained with o-dianisidine.

A most common β chain variant is Hb-E. Another common anomaly is α-thalassemia, the presence of which results in significant quantities of Hb-Bart's or γ_4. Figure 5-13 gives examples of electrophoretic examinations that have been obtained. It appears that the amount of Hb-Bart's is directly related to the severity of the α-thalassemia; the incidence of Hb-Bart's in neonates is over 20%. Besides Hb-Bart's a slow-moving α chain variant, Hb-Constant Spring or Hb-Thai, can be present (see Chapters 4 and 6 for details). A recent review of his data has led Dr. Pootrakul to conclusions regarding the genotypic expression of the α-thalassemia syndrome which are summarized in Table 5-10. The incidence of these conditions in the various populations remain to be determined.

*Data were supplied by Dr. S. Pootrakul, Bangkok, Thailand (deceased).